

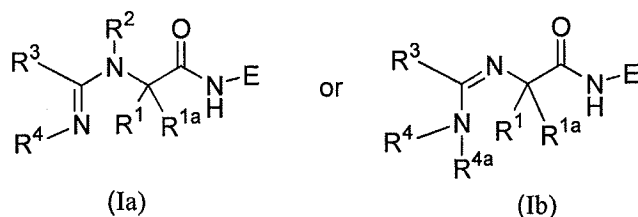
EXAMINER'S AMENDMENT

~~Amendments to the Claims:~~

~~This listing of claims will replace all prior versions, and listings of claims in the application.~~

Listing of Claims:

1. **(Currently Amended)** A compound of Formula (Ia) or (Ib):



wherein:

E is:

- (i) ~~—C(R⁵)(R⁶)X¹ where X¹ is CHO, —C(R⁷)(R⁸)CF₃, —C(R⁷)(R⁸)CF₂CF₂R⁹, —C(R⁷)(R⁸)R¹⁰, —CH=CHS(O)₂R¹⁰, —C(R⁷)(R⁸)C(R⁷)(R⁸)OR¹⁰, —C(R⁷)(R⁸)CH₂OR¹⁰, —C(R⁷)(R⁸)C(R⁷)(R⁸)R¹⁰, —C(R⁷)(R⁸)CH₂N(R¹¹)SO₂R¹⁰, —C(R⁷)(R⁸)CF₂C(O)NR¹⁰R¹¹, —C(R⁷)(R⁸)C(O)NR¹⁰R¹¹, —C(R⁷)(R⁸)C(O)N(R¹¹)(CH₂)₂OR¹¹, —C(R⁷)(R⁸)C(O)N(R¹¹)(CH₂)₂NR¹⁰R¹¹; or~~
- (ii) —C(R^{5a})(R^{6a})CN;

where:

R⁵ and R^{5a} are independently is hydrogen or alkyl; and

R⁶ and R^{6a} are independently is selected from the group consisting of hydrogen, alkyl, haloalkyl, carboxyalkyl, alkoxycarbonylalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl, heterocyclylalkyl, cyano, -alkylene-X-R¹² (where X is —O—, —NR¹³—, —CONR¹³—, —S(O)_{n1}—, —NHCO—, —CO—, or —C(O)O— where n1 is 0-2, and R¹² and R¹³ are independently hydrogen, alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heteroaryl, or heteroaralkyl) wherein the aromatic or alicyclic ring in R⁶ and R^{6a} is optionally substituted with one, two, or three R^a independently selected from alkyl, haloalkyl, alkoxy,

hydroxy, haloalkoxy, halo, carboxy, alkoxycarbonyl, amino, monsubstituted amino, disubstituted amino, nitro, aryloxy, benzyloxy, acyl, or arylsulfonyl where the aromatic or alicyclic ring in R^a is optionally substituted with one or two substituents independently selected from alkyl, halo, alkoxy, haloalkyl, haloalkoxy, hydroxy, amino, alkylamino, dialkylamino, carboxy, or alkoxycarbonyl; or

~~R⁵ and R⁶ and R^{5a} and R^{6a}~~ taken together with the carbon atom to which both ~~R⁵ and R⁶~~ and R^{5a} and R^{6a} are attached form (i) cycloalkylene optionally substituted with one or two R^b independently selected from alkyl, halo, alkylamino, dialkylamino, aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heteroaryl, heteroaralkyl, alkoxycarbonyl, or aryloxycarbonyl, or (ii) heterocycloalkylene optionally substituted with one to four R^c which are independently selected from alkyl, haloalkyl, hydroxy, hydroxyalkyl, alkoxyalkyl, alkoxyalkyloxyalkyl, aryloxyalkyl, heteroaryloxyalkyl, aminoalkyl, acyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl, heterocyclylalkyl, cycloalkyl, cycloalkylalkyl, -S(O)_{n2}R¹⁴, -alkylene-S(O)_{n2}-R¹⁵, -COOR¹⁶, -alkylene-COOR¹⁷, -CONHR¹⁸R¹⁹, or -alkylene-CONHR²⁰R²¹ (where n2 is 0-2 and R¹⁴-R¹⁷, R¹⁸ and R²⁰ are independently hydrogen, alkyl, haloalkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, cycloalkyl, cycloalkylalkyl, or heterocyclyl and R¹⁹ and R²¹ are independently hydrogen or alkyl) wherein the aromatic or alicyclic ring in the groups attached to cycloalkylene or heterocycloalkylene is optionally substituted with one, two, or three substituents independently selected from alkyl, haloalkyl, alkoxy, hydroxy, haloalkoxy, halo, carboxy, alkoxycarbonyl, amino, monsubstituted amino, disubstituted amino, or acyl;

~~R⁷ is hydrogen or alkyl;~~

~~R⁸ is hydroxy; or~~

~~R⁷ and R⁸ together form oxo;~~

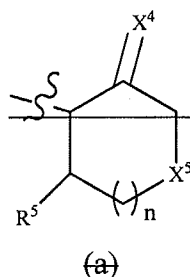
~~R⁹ is hydrogen, halo, alkyl, aralkyl or heteroaralkyl; and~~

~~R¹⁰ is alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, or heterocyclylalkyl wherein the aromatic or alicyclic ring in R¹⁰ is optionally substituted with one, two, or three R^d independently selected from alkyl, haloalkyl, alkoxy, cycloalkyl, hydroxy, haloalkoxy, halo, carboxy, alkoxycarbonyl, aryl, heteroaryl, amino, monsubstituted amino, disubstituted amino, or acyl wherein the aromatic or alicyclic ring in R^d is~~

~~optionally substituted with one, two, or three substituents independently selected from alkyl, haloalkyl, alkoxy, haloalkoxy, halo, hydroxy, carboxy, alkoxy-carbonyl, amino, alkylamino, or dialkylamino; and~~

R^{11} is hydrogen or alkyl; or

(iii) — a group of formula (a):



where:

n is 0, 1, or 2;

X^4 is selected from NR^{22} , S , or O where R^{22} is hydrogen, alkyl, or alkoxy; and

X^5 is O , S , SO_2 , or NR^{23} where R^{23} is selected from hydrogen, alkyl, haloalkyl, hydroxyalkyl, alkoxyalkyl, aryloxyalkyl, heteroaryloxyalkyl, aminoalkyl, acyl, aryl, aralkyl, heteroaryl, heteroaralkyl, cycloalkyl, cycloalkylalkyl, $S(O)_2R^{24}$, alkylene- $S(O)_nR^{25}$, $COOR^{26}$, alkylene- $COOR^{27}$, $CONR^{28}R^{29}$, or alkylene- $CONR^{30}R^{31}$ (where n is 0-2 and R^{24} , R^{27} , R^{28} and R^{30} are independently hydrogen, alkyl, haloalkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, or heterocyclylalkyl and R^{29} and R^{31} are independently hydrogen or alkyl) where the aromatic or alicyclic ring in X^5 is optionally substituted with one, two, or three substituents independently selected from alkyl, haloalkyl, alkoxy, haloalkoxy, halo, hydroxy, amino, alkylamino, dialkylamino, carboxy, or alkoxy-carbonyl;

R^5 is as defined above;

R^1 is hydrogen or alkyl;

R^{1a} is hydrogen, alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclylalkyl, or $-alkylene-X-R^{32}$ [wherein X is NR^{33} , $-O-$, $-S(O)_n$, $-CO-$, $-COO-$, $-OCO-$, $-NR^{33}CO-$, $-CONR^{33}$, $-NR^{33}SO_2-$, $-SO_2NR^{33}$, $-NR^{33}COO-$, $-OCONR^{33}$, $-NR^{33}CONR^{34}$, or $-NR^{33}SO_2NR^{34}$ (where R^{33} and R^{34} are independently hydrogen, alkyl, or acyl

and n_4 is 0-2) and R^{32} is hydrogen, alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl, or heterocyclylalkyl] wherein said alkylene chain is optionally substituted with one to six halo and wherein the aromatic or alicyclic ring in R^{1a} is optionally substituted with one, two, or three R^c independently selected from alkyl, haloalkyl, alkoxy, hydroxy, haloalkoxy, halo, nitro, cyano, carboxy, alkoxycarbonyl, aryl, heteroaryl, cycloalkyl, cycloalkylalkyl, aralkyl, heteroaralkyl, amino, monosubstituted amino, disubstituted amino, or acyl; or

~~R^+ and R^{1a} together with the carbon atoms to which they are attached form cycloalkylene or heterocycloalkylene ring wherein said cycloalkylene or heterocycloalkylene is optionally substituted with one or two R^f independently selected from alkyl, halo, hydroxyalkyl, keto, or SO_2R^{39} where R^{39} is alkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heteroaryl or heteroaralkyl where the aromatic or alicyclic ring in R^f is optionally substituted with one, two, or three substituents independently selected from alkyl, alkoxy, haloalkyl, haloalkoxy, hydroxy, halo, carboxy, or alkoxycarbonyl;~~

R^2 is hydrogen or alkyl;

R^3 is hydrogen, alkyl, haloalkyl, cycloalkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl, heterocyclylalkyl, amino, mono or disubstituted amino, or $-alkylene-X^3-R^{35}$ [wherein X^3 is $-NR^{36}-$, $-O-$, $-S(O)_{n5}-$, $-CO-$, $-COO-$, $-OCO-$, $-NR^{36}CO-$, $-CONR^{36}-$, $-NR^{36}SO_2-$, $-SO_2NR^{36}-$, $-NR^{36}COO-$, $-OCONR^{36}-$, $-NR^{36}CONR^{37}-$, or $-NR^{36}SO_2NR^{37}-$ (where R^{36} and R^{37} are independently hydrogen, alkyl, or acyl and n_5 is 0-2) and R^{35} is hydrogen, alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heteroaryl, or heteroaralkyl] wherein the aromatic or alicyclic rings in R^3 are optionally substituted by one, two, or three R^g independently selected from alkyl, halo, hydroxy, alkoxy, haloalkyl, haloalkoxy, oxo, cyano, nitro, acyl, acyloxy, aryl, heteroaryl, cycloalkyl, heterocyclyl, aryloxy, benzyloxy, carboxy, alkoxycarbonyl, aryloxycarbonyl, carbamoyl, alkylthio, alkylsulfinyl, alkylsulfonyl, arylthio, arylsulfonyl, arylsulfinyl, alkoxycarbonylamino, aryloxycarbonylamino, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl, amino, monosubstituted or disubstituted amino, and further wherein the aromatic and alicyclic rings in R^g are optionally substituted with one, two, or



three R^h wherein R^h is independently selected from alkyl, halo, haloalkyl, haloalkoxy, hydroxy, nitro, cyano, hydroxyalkyl, alkoxy, alkoxyalkyl, aminoalkyl, alkylthio, alkylsulfonyl, amino, alkylamino, dialkylamino, aryl, heteroaryl, cycloalkyl, carboxy, carboxamido, or alkoxycarbonyl;

R^4 is $-S(O)_2R^{38}$ where R^{38} is phenyl or naphthyl optionally substituted with one, two, or three R^i independently selected from alkyl, alkoxy, halo, haloalkyl, haloalkoxy, hydroxy, alkylthio, alkylsulfonyl, arylsulfonyl, aminosulfonyl, acyl, amino, monosubstituted amino, disubstituted amino, carboxy, alkoxycarbonyl, hydroxyalkyl, alkoxyalkyl, aminoalkyl, aryl, heteroaryl, heterocyclyl, aryloxycarbonyl, heteroaryloxycarbonyl, aryloxy, heteroaryloxy, $-NHSO_2R^j$ where R^j is alkyl, aryl, or heteroaryl, $-SO_2NR^kR^l$ where R^k is hydrogen or alkyl and R^l is alkyl, aryl, heteroaryl, hydroxyalkyl, alkoxyalkyl, or aminoalkyl, $-NHCOOR^m$ where R^m is alkyl, aryl, or heteroaryl, or $-NHCONR^nR^o$ where R^n and R^o are independently hydrogen, alkyl, aryl, aralkyl, heteroaryl, or heteroaralkyl; where the aromatic or alicyclic ring in R^i is optionally substituted with one or two substituents independently selected from alkyl, halo, alkoxy, haloalkyl, haloalkoxy, hydroxy, amino, alkylamino, dialkylamino, carboxy, or alkoxycarbonyl;

R^{4a} is hydrogen, alkyl, halo, haloalkyl, haloalkyl, hydroxyalkyl, alkoxyalkyl, alkoxy, hydroxy, aryl, aralkyl, aroyl, heteroaryl, heteraralkyl, heteroaroyl, $-C(O)OR^{40}$ where (R^{40} is hydrogen, alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, heteroaryl, heteroarylalkyl, aryl, or aralkyl), alkylsulfonyl, arylsulfonyl, heteroarylsulfonyl, alkylaminosulfonyl, arylaminosulfonyl, or cycloalkyl wherein the aromatic rings in R^{4a} are optionally substituted with one, two or three halogen, hydroxy, alkyl, alkoxy, haloalkyl, haloalkoxy, carboxy, nitrile, nitro, or $-CONH_2$; or a pharmaceutically acceptable salts thereof.

2. (Original) The compound of Claim 1 wherein R^4 is $-S(O)_2R^{38}$ where R^{38} is phenyl or naphthyl optionally substituted with one, two, or three R^i independently selected from alkyl, alkoxy, halo, haloalkyl, haloalkoxy, hydroxy, alkylthio, alkylsulfonyl, arylsulfonyl, aminosulfonyl, acyl, amino, monosubstituted amino, disubstituted amino, carboxy, alkoxycarbonyl, hydroxyalkyl, alkoxyalkyl, aminoalkyl, aryl, heteroaryl, or heterocyclyl where the aromatic or alicyclic ring in R^i is optionally substituted with one or two substituents

independently selected from alkyl, halo, alkoxy, haloalkyl, haloalkoxy, hydroxy, amino, alkylamino, dialkylamino, carboxy, or alkoxycarbonyl.

3. (Canceled)

4. (Canceled)

5. (Canceled)

6. (Canceled)

³
~~7.~~ (Currently amended) The compound of Claim 1 ~~or 2~~ wherein E is $-CR^{5a}R^{6a}CN$ where R^{5a} and R^{6a} together with the carbon atom to which they are attached form cycloalkylene optionally substituted with one or two R^b independently selected from alkyl, halo, dialkylamino, aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heteroaryl, heteroaralkyl, alkoxycarbonyl, or aryloxycarbonyl.

⁴
~~8.~~ (Currently amended) The compound of Claim 1 ~~or 2~~ wherein E is $-CR^{5a}R^{6a}CN$ where R^{5a} and R^{6a} together with the carbon atom to which they are attached form cyclopropylene, cyclobutylene, cyclopentylene, or cyclohexylene optionally substituted with one or two R^b independently selected from alkyl, halo, dialkylamino, aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heteroaryl, heteroaralkyl, alkoxycarbonyl, or aryloxycarbonyl.

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~~9.~~ (Currently amended) The compound of Claim 1 ~~or 2~~ wherein E is $-CR^{5a}R^{6a}CN$ where R^{5a} and R^{6a} together with the carbon atom to which they are attached form heterocycloalkylene optionally substituted with one to two R^c which are independently selected from alkyl, haloalkyl, hydroxyalkyl, alkoxyalkyl, aryloxyalkyl, heteroaryloxyalkyl, aminoalkyl, acyl, aryl, aralkyl, heteroaryl, heteroaralkyl, cycloalkyl, cycloalkylalkyl, $-S(O)_{n2}R^{14}$, $-alkylene-S(O)_{n2}-R^{15}$, $-COOR^{16}$, $-alkylene-COOR^{17}$, $-CONHR^{18}R^{19}$, or $-alkylene-CONHR^{20}R^{21}$ (where $n2$ is 0-2 and $R^{14}-R^{17}$, R^{18} and R^{20} are independently hydrogen, alkyl, haloalkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, cycloalkyl, cycloalkylalkyl, or heterocyclyl and R^{19} and R^{21} are independently hydrogen or alkyl) wherein the aromatic or alicyclic ring in the groups attached to

heterocycloalkylene is optionally substituted with one, two, or three substituents independently selected from alkyl, haloalkyl, alkoxy, hydroxy, haloalkoxy, halo, carboxy, alkoxycarbonyl, amino, monsubstituted amino, disubstituted amino, or acyl.

10. (Canceled)

⁶
~~11.~~ (Currently amended) The compound of any of the Claims ¹⁻⁵ ~~1-10~~ 1, 2, 7, 8 or 9,
wherein:

R¹ is hydrogen; and

R^{1a} is alkyl, cycloalkyl, aralkyl, heteroaralkyl, cycloalkylalkyl, heterocyclylalkyl, or -alkylene-X-R³² [wherein X is -NR³³-, -O-, -S(O)_{n4}-, -CO-, -COO-, -OCO-, -NR³³CO-, -CONR³³-, -NR³³SO₂-, -SO₂NR³³-, -NR³³COO-, -OCONR³³-, -NR³³CONR³⁴, or -NR³³SO₂NR³⁴- (where R³³ and R³⁴ are independently hydrogen, alkyl, or acyl and n4 is 0-2) and R³² is hydrogen, alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl, or heterocyclylalkyl] wherein said alkylene chain is optionally substituted with one to six halo and wherein the aromatic or alicyclic ring in R^{1a} is optionally substituted with one, two, or three R^e independently selected from alkyl, haloalkyl, alkoxy, hydroxy, haloalkoxy, halo, nitro, cyano, carboxy, alkoxycarbonyl, aryl, heteroaryl, cycloalkyl, cycloalkylalkyl, aralkyl, heteroaralkyl, amino, monsubstituted amino, disubstituted amino, or acyl.

⁷
~~12.~~ (Currently amended) The compound of any of the Claims ¹⁻⁵ ~~1-10~~ 1, 2, 7, 8 or 9,
wherein:

R^{1a} is 2-methylpropyl, 2,2-dimethylpropyl, 4,4-dimethylcyclohexylmethyl, 4-ethyl-4-methylcyclohexylmethyl, 4,4-diethylcyclohexylmethyl, 3,3-dimethylcyclohexylmethyl, 3,5-dimethylcyclohexylmethyl, 1-ethoxycarbonylpiperidin-4-ylmethyl, 1-methylpiperidin-4-ylmethyl, cycloheptylmethyl, cyclooctylmethyl, 3,3-dimethylbutyl, 3-methylbutyl, 2-cyclohexylethyl, 2,2,3-trimethylbutyl, 2-cyclohexyl-2-methylpropyl, 3,3-dimethylpentyl, 3-ethyl-3-methylpentyl, 2-(1-methylcyclohexyl)ethyl, tetrahydronaphthylmethyl, 2-tetrahydropyran-4-ylethyl, 2-(1-methylcyclopropyl)ethyl, 2-(1-methylcyclopropyl)-2-methylpropyl, 2-

cyclopentylethyl, 2-cyclopentyl-2-methylpropyl, 4-isopropyl-4-methylcyclohexylmethyl, phenylmethanethiomethyl, phenylmethanesulfinylmethyl, dimethylaminomethyl, pyrrolidin-1-ylmethyl, piperidin-1-ylmethyl, morpholin-4-ylmethyl, thiomorpholin-4-ylmethyl, 1-oxo-thiomorpholin-4-ylmethyl, 1,1-dioxothiomorpholin-4-ylmethyl, tetrahydrothiopyran-4-ylmethyl, 1-oxotetrahydrothiopyran-4-ylmethyl, 1,1-dioxotetrahydrothiopyran-4-ylmethyl, 1-methylpiperazin-4-ylmethyl, benzyloxymethyl, n-butyl, ethoxymethyl, ethylthiomethyl, ethylsulfinylmethyl, ethylsulfonylmethyl, isopropylthiomethyl, isopropylloxymethyl, 2-dimethylaminoethyl, 2-piperidin-1-ylethyl, 2-pyrrolidin-1-ylethyl, 2-methylthioethyl, 2-methylsulfinylethyl, 2-methylsulfonylethyl, *tert*-butylthiomethyl, *tert*-butyloxymethyl, benzyl, 4-methoxybenzyl, imidazol-4-ylmethyl, 4-dimethylaminobutyl, indol-3-ylmethyl, 2-dimethylaminocarbonylethyl, 2-pyrrolidin-1-ylcarbonylethyl, dimethylaminocarbonylmethyl, pyrrolidin-1-ylcarbonylmethyl, methoxycarbonylmethyl, 2-fluorophenylmethanesulfonylmethyl, 2-chlorophenylmethanesulfonylmethyl, 2-nitrophenylmethanesulfonylmethyl, 2-cyanophenylmethanesulfonylmethyl, pyridin-3-ylmethanesulfonylmethyl, pyridin-2-ylmethanesulfonylmethyl, pyridin-4-ylmethanesulfonylmethyl, 2-fluorophenylmethanethiomethyl, 2-chlorophenylmethanethiomethyl, 2-cyanophenylmethanethiomethyl, 2-nitrophenylmethanethiomethyl, cyclohexylmethanethiomethyl, cyclohexylsulfinylthiomethyl, cyclohexylmethanesulfonylmethyl, 3,4-dichlorobenzyl, 2-chlorobenzyl, 4-ethoxybenzyl, 4-nitrobenzyl, biphen-4-ylmethyl, naphth-1-ylmethyl, 2-methylbutyl, 1-methylpropyl, naphth-2-ylmethyl, 4-chlorobenzyl, 3-chlorobenzyl, 4-fluorobenzyl, indol-2-ylmethyl, 1-benzylimidazol-4-ylmethyl, 2-phenethyl, 4-hydroxybenzyl, 2-(4-hydroxyphenyl)ethyl, 4-ethyl-4-methylpiperidin-1-ylmethyl, 2-methylcyclohexylmethyl, 4-methoxycyclohexylmethyl, indol-1-ylmethyl, 1-methylpiperidin-2-ylmethyl, 2-bicyclo[2.2.1]hept-3-ylethyl, 8-methyl-8-azabicyclo[3.2.1]oct-3-ylmethyl, bicyclo[3.2.1]oct-3-ylmethyl, bicyclo[3.1.1]hept-3-ylmethyl, 6,6-dimethylbicyclo[3.1.1]hept-3-ylmethyl, 6,6-dimethylbicyclo[3.1.1]hept-4-ylmethyl, 2-bicyclo[2.2.1]hept-1-ylethyl, bicyclo[2.2.1]hept-2-ylethyl, thiophene-2-sulfonylmethyl, 3-chloro-2-fluorophenylmethane-sulfonylmethyl, benzenesulfonylmethyl, phenylmethanesulfonylmethyl, 2-benzenesulfonylethyl, 2-(pyridin-2-ylsulfonyl)ethyl, 2-(pyridin-4-ylsulfonyl)ethyl, 2-phenylmethanesulfonyl-ethyl,

oxypyridin-2-ylmethanesulfonylmethyl, 4-methoxyphenyl-methanesulfonylmethyl, *p*-tolylmethanesulfonylmethyl, 4-chlorophenylmethanesulfonylmethyl, *o*-tolylmethanesulfonylmethyl, 3,5-dimethylphenylmethanesulfonylmethyl, 4-trifluoromethylphenylmethanesulfonylmethyl, 4-trifluoromethoxyphenylmethanesulfonylmethyl, 2-bromophenylmethanesulfonylmethyl, naphth-2-ylmethanesulfonylmethyl, 3-methylphenylmethanesulfonylmethyl, 3-trifluoromethylphenylmethanesulfonylmethyl, 3-trifluoromethoxyphenylmethane-sulfonylmethyl, 4-fluoro-2-trifluoromethoxyphenylmethanesulfonylmethyl, 2-fluoro-6-trifluoromethylphenylmethanesulfonylmethyl, 2,6-difluorobenzyl, 1-methylcyclopentylmethyl, cyclohexyl, pyridin-4-ylmethyl, 3-chlorophenylmethanesulfonylmethyl, 2-trifluoromethylphenylmethanesulfonylmethyl, 4-*tert*-butylphenylmethanesulfonylmethyl, 2-fluoro-3-methylphenylmethanesulfonyl-methyl, 3-fluorophenylmethanesulfonylmethyl, 4-fluorophenylmethanesulfonylmethyl, 2,5-difluorophenylmethanesulfonylmethyl, 2,6-difluorophenylmethanesulfonylmethyl, 2,5-dichlorophenylmethanesulfonylmethyl, 3,4-dichlorophenylmethanesulfonylmethyl, 2-(1,1-difluoromethoxy)phenylmethanesulfonylmethyl, 3-cyanophenylmethane-sulfonylmethyl, 2-trifluoromethoxyphenylmethanesulfonylmethyl, 3-trifluoromethoxyphenylmethanesulfonylmethyl, 2,3-difluorophenylmethane-sulfonylmethyl, 2,5-difluorophenylmethanesulfonylmethyl, biphenyl-2-ylmethane-sulfonylmethyl, cyclohexylmethyl, 3-fluorophenyl-methanesulfonylmethyl, 2-pyridin-2-ylsulfonylethyl, 2-phenylsulfonylethyl, 2,2-difluoro-3-phenylpropyl, 2,2-dichloro-3-phenylpropyl, 2,2,2-trichloroethyl, 2,2-dichloroethyl, 1,4-dimethylcyclopentylmethyl, 3,4-difluorophenylmethanesulfonylmethyl, 2,4-difluorophenylmethanesulfonylmethyl, 2,4,6-trifluorophenylmethanesulfonylmethyl, 2,4,5-trifluorophenylmethanesulfonylmethyl, 2,3,4-trifluorophenylmethanesulfonylmethyl, 2,3,5-trifluorophenylmethanesulfonylmethyl, 2,5,6-trifluorophenylmethanesulfonyl-methyl, 2-chloro-5-trifluoromethylphenylmethane-sulfonylmethyl, 2-methylpropane-1-sulfonylmethyl, 2-fluoro-3-trifluoromethylphenyl-methanesulfonylmethyl, 2-fluoro-4-trifluoromethylphenylmethanesulfonylmethyl, 2-fluoro-5-trifluoromethyl-phenylmethanesulfonylmethyl, 4-fluoro-3-trifluoromethyl-

phenylmethanesulfonylmethyl, 2-methoxyphenylmethanesulfonylmethyl, 3,5-bis-trifluoromethylphenyl-methanesulfonylmethyl, 4-difluoromethoxyphenylmethanesulfonylmethyl, 3-difluoromethoxyphenylmethanesulfonylmethyl, 2,6-dichlorophenylmethanesulfonylmethyl, biphenyl-4-ylmethanesulfonylmethyl, 3,5-dimethyl-isoxazol-4-ylmethanesulfonylmethyl, 5-chlorothien-2-ylmethane-sulfonylmethyl, 2-[4-(1,1-difluoromethoxy)benzenesulfonyl]ethyl, 2-[2-(1,1-difluoromethoxy)benzenesulfonyl]ethyl, 2-[3-(1,1-difluoromethoxy)benzenesulfonyl]ethyl, 2-(4-trifluoromethoxybenzenesulfonyl)ethyl, 2-(3-trifluoromethoxybenzenesulfonyl)-ethyl, 2-(2-trifluoromethoxybenzenesulfonyl)-ethyl, (cyanomethylmethylcarbamoyl)methyl, biphenyl-3-ylmethyl, 2-oxo-2-pyrrolidin-1-ylethyl, 2-benzenesulfonylethyl, isobutylsulfanylmethyl, 2-phenylsulfanylethyl, cyclohexylmethanesulfonylmethyl, 2-cyclohexylethanesulfonyl, benzyl, naphth-2-yl, phenylmethanesulfanylmethyl, 2-trifluoromethylphenylmethanesulfanylmethyl, phenylsulfanylethyl, cyclopropylmethanesulfonylmethyl, 2-methylpropylsulfonylmethyl, 5-bromothien-2-ylmethyl, 3-phenylpropyl, 2,2-difluoro-3-phenylpropyl, 3,4,5-trimethoxy-phenylmethanesulfonyl-methyl, 2,2-difluoro-3-thien-2-ylpropyl, cyclohexylethyl, cyclohexylmethyl, cyclopentylmethyl, *tert*-butylmethyl, 1-methylcyclohexylmethyl, 1-methylcyclopentylmethyl, 2,2-difluoro-3-phenylpropyl, 2,2-dimethyl-3-phenylpropyl, 1-benzylcyclopropylmethyl, or benzyloxymethyl; and

R¹ is hydrogen.

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~~13.~~ (Currently amended) The compound of any of the Claims ¹⁻⁵~~1-12~~ 1, 2, 7, 8 or 9,
wherein:

R³ is hydrogen, alkyl, cycloalkyl, phenyl, benzyl, naphthyl, alkylSO₂alkyl, cycloalkylSO₂alkyl, arylSO₂alkyl, pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl, indolinyl, pyranyl, thiopyranyl, furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, isoxazolyl, pyrimidinyl, pyrazinyl, pyridazinyl, indolyl, quinolinyl, benzofuranyl, benzthienyl, benzimidazolyl, benzthiazolyl, benzoisoxazolyl, benzoxazolyl or

amino; wherein the aromatic or alicyclic ring in R³ is optionally substituted by one, two, or three R^g;

each R^g is independently alkyl, halo, hydroxy, oxo, carboxy, cyano, nitro, carboxamide, cycloalkyl, phenyl, naphthyl, pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl, furanyl, thienyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, alkoxy, -COR (where R is alkyl), -OC(O)R (where R is alkoxy or aryl), aryloxy, benzyloxy, alkoxycarbonyl, aryloxycarbonyl, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl, furanyl, thienyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl or quinoxalinyl, -NHCOR (where R is alkyl or aryl), alkylthio, arylthio, alkylsulfanyl, alkylsulfonyl, arylsulfanyl, arylsulfonyl, alkoxycarbonylamino, aryloxycarbonylamino, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl, furanyl, thienyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl or quinoxalinyl, where the aromatic or alicyclic rings in R^g may be further optionally substituted by one, two or three R^h independently selected from alkyl, aryl, cycloalkyl, alkoxy, haloalkyl, haloalkoxy, halo, hydroxy, carboxy, carboxamido, cyano, or nitro;

R² is hydrogen or methyl; and

R^{4a} is hydrogen, alkyl, cycloalkyl, aryl, alkoxy, or hydroxy.

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14. (Currently amended) The compound of any of the Claims 1-12 ¹⁻⁵ ~~1, 2, 7, 8 or 9~~,
wherein: [^]

R^3 is hydrogen, methyl, ethyl, isopropyl, cyclopropyl, cyclopentyl, cyclohexyl, phenyl, benzyl, naphthyl, pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl, furanyl, thienyl, thiazolyl, imidazolyl, pyridinyl, pyrazinyl, or amino where the nitrogen atom is mono or disubstituted with alkyl and wherein the aromatic or alicyclic rings in R^3 are optionally substituted with one, two, or three R^g independently selected from methyl ethyl, fluoro, chloro, bromo, iodo, hydroxy, oxo, carboxy, cyano, nitro, carboxamide, cyclopropyl, phenyl, pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl, thienyl imidazolyl, methoxy, acetyl, acetoxo, phenoxy, benzyloxy, methoxycarbonyl, phenoxycarbonyl, benzoyloxy, carbamoyl wherein the nitrogen atom is mono or disubstituted independently with methyl, ethyl or phenyl, acetylamino, benzoylamino, methylthio, phenylthio, phenylsulfonyl, methylsulfonyl, methoxycarbonylamino, phenoxycarbonylamino, methylcarbamoyloxy, phenylcarbamoyloxy, methylsulfonylamino, phenylsulfonylamino, methylaminosulfonyl, phenylaminosulfonyl, amino wherein the nitrogen atom is mono or disubstituted independently with methyl or phenyl; wherein the aromatic or alicyclic rings in R^g are further optionally substituted with one, two, or three R^h independently selected from methyl, cyclopropyl, phenyl, methoxy, fluoro, chloro, hydroxy, carboxy or carboxamido.

¹⁰
15. (Currently amended) The compound of any of the Claims ¹⁻⁵~~1-12, 1, 2, 7, 8 or 9;~~
wherein:

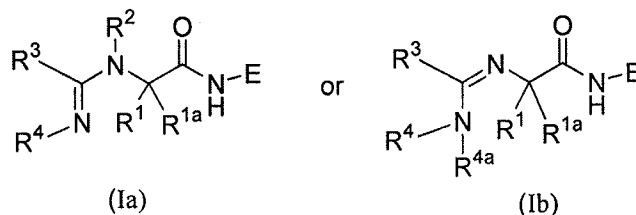
R^3 is hydrogen, methyl, carboxy, ethyl isopropyl, cyclopropyl, cyclohexyl, phenyl, benzyl, naphthyl, pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, furanyl, thientyl, thiazolyl, imidazoly, pyridinyl, pyrazinyl or amino where the nitrogen atom is optionally substituted with alkyl and wherein the aromatic or alicyclic rings in R^3 are optionally substituted with one, two, or three R^g independently selected from methyl, chloro, fluoro, phenyl, thienyl, methoxy, acetyl, acetoxo, phenoxy, benzyloxy, methoxycarbonyl, carbamoy wherein the nitrogen atom is mono or disubstitued independently with methyl or phenyl, acetylamino, methylthio, phenylthio, phenylsulfonyl, methylsulfonyl, methoxycarbonylamino, methylcarbamoyloxy, phenylcarbamoyloxy, methylsulfonylamino, phenylsulfonylamino, amino wherein the nitrogen atom is mono or disubstituted independently with methyl or phenyl;

R^{4a} is hydrogen, alkyl or alkoxy; and

R^4 is $-S(O)_2R^{38}$ where R^{38} is phenyl or naphthyl optionally substituted with one, two, or three R^i independently selected from alkyl, alkoxy, halo, haloalkyl, haloalkoxy, hydroxy, alkylthio, alkylsulfonyl, aminosulfonyl, acyl, amino, monosubstituted amino, disubstituted amino, hydroxyalkyl, alkoxyalkyl, aminoalkyl, aryl, heteroaryl, or heterocyclyl where the aromatic or alicyclic ring in R^i is optionally substituted with one or two substituents independently selected from alkyl, halo, alkoxy, haloalkyl, haloalkoxy, hydroxy, amino, alkylamino, dialkylamino, carboxy, or alkoxycarbonyl.

¹¹
~~16.~~ (Currently amended) The compound of any of the Claims ¹⁻⁵~~1-15, 1, 2, 7, 8 or 9,~~ where R^4 is $-S(O)_2R^{38}$ where R^{38} is phenyl optionally substituted with one, two, or three R^i independently selected from alkyl, alkoxy, halo, haloalkyl, haloalkoxy, hydroxy, alkylthio, alkylsulfonyl, aminosulfonyl, acyl, amino, monosubstituted amino, disubstituted amino, hydroxyalkyl, alkoxyalkyl, aminoalkyl, aryl, heteroaryl, or heterocyclyl where the aromatic or alicyclic ring in R^i is optionally substituted with one or two substituents independently selected from alkyl, halo, alkoxy, haloalkyl, haloalkoxy, hydroxy, amino, alkylamino, dialkylamino, carboxy, or alkoxycarbonyl.

¹²
~~17.~~ (Currently amended) A compound of formula:



wherein:

R^1 , R^2 , and R^{4a} are hydrogen;


R^{1a} is cycloalkylalkyl wherein the alicyclic ring is optionally substituted with alkyl, heteroaralkyl, or $-alkylene-S(O)_{n4}-R^{32}$ where $n4$ is 0 to 2 and R^{32} is aralkyl where the aromatic ring is optionally substituted with haloalkoxy;

R³ is hydrogen, alkyl, heterocyclyl, or alkylthio;

R⁴ is phenylsulfonyl;

E is -CHR⁶COR¹⁰ where R⁶ is alkyl and R¹⁰ is heteroaryl optionally substituted with alkyl or aryl, -CH₂CN, or -CR^{5a}R^{6a}-CR^{5a}R^{6a}CN where R^{5a} and R^{6a} together with the carbon atom to which they are attached form cycloalkylene or heterocycloalkylene; or
a pharmaceutically acceptable salt thereof.

¹³
~~18.~~ (Currently amended) A pharmaceutical composition comprising a compound of any of the Claims ~~1-17~~¹⁻⁵ ~~1, 2, 7, 8, 9~~¹² or ~~17~~ in admixture with one or more suitable excipients.

¹⁴
 ~~19.~~ (Currently amended) A method for treating a ^{psoriasis} ~~disease~~ in an animal mediated by ~~cysteine proteases~~ which method comprises administering to the animal a therapeutically effective amount of a compound of any of the Claims ~~1-17~~¹⁻⁵ ~~1, 2, 7, 8, 9~~¹² or ~~17~~.

~~20. (Original) The method of Claim 19 wherein the disease is psoriasis.~~